REMARKS

Introduction

As an initial matter, applicant thanks Examiner Gupta and his supervisor, Examiner Brumback, for the courtesies extended by them during an interview with applicant's representative on January 5, 2004. The following remarks reflect the content of that interview.

Receipt is acknowledged of a non-final office action dated September 24, 2003. In the action, the examiner rejected claims 1-10, 16 and 18-47 for alleged nonenablement.

Status of the Claims

In this amendment, applicant amended claim 26 and added new claims 48-50. Support for amended claim 26 can be found in example 2, and support for the new claims can be found in example 2 and on page 7, paragraph 0017 of the instant specification. Upon entry of this amendment, claims 1-10, 16, and 18-50 will be pending.

35 U.S.C. § 112, 1st paragraph

The examiner rejects claims 1-10, 16 and 18-47 for alleged non-enablement. In particular, the examiner asserts that "it is unclear as to the 'ordinary meaning' of Null IGF" and that "[s]tructurally speaking, it is unclear what modification in the IGF would render an IGF molecule a 'null IGF.'" (office action at 3, emphasis added).

Applicant respectfully disagrees. The specification describes precise modifications that can be made to an IGF molecule to render it "null," and discloses references which illustrate exemplary null IGFs (see, specification at page 7). In addition, many of the claims are directed to a defined subset of null IGF molecules and in fact, recite very specific amino acid substitutions. Thus, the claimed invention clearly defines what IGF structural modifications fall within the scope of the claims.

In addition, the examiner states that "one of ordinary skill in the [art] does not readily know which modification would lead to the desired functional activity" and that "the functional definition does not provide any guidance as to the structural definition" (office action at 4). As discussed above, applicant's claims recite null IGF compounds with specific

structural features. As such, many of the claims do not solely recite the functional definition of a null IGF.

Moreover, according to the PTO's own rules, "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement...is satisfied" (M.P.E.P. § 2164.01, *citing In re Fisher*, 427 F.2d 833 (CCPA 1970)). Indeed, example 2 of the present specification describes the use of a Y60L null IGF for the treatment of prostate cancer *in vivo* (specification at 14-15).

Furthermore, one of skill in the art would predict that replacing tyrosine at position 60 with any residue, or at the very least with any non-aromatic residue, would also disrupt IGF receptor binding. Since tyrosine at position 60 is needed to preserve normal IGF-I binding to they type 1 and type 2 receptors, changing this residue will alter normal IGF-I activity. In fact, Bayne teaches that Tyr^{60} is "involved in the high affinity binding of IGF-I to the type 1 IGF receptor...[and] for maintaining binding to the type 2 IGF receptor" (Bayne *et al.*, *J. Biol. Chem.* 15648-15652 (1990), abstract). *See*, Exhibit A. Bayne further teaches that Tyr^{60} of IGF-I is analogous to Tyr^{A19} of insulin, and that mutations in A19 "result in dramatic loss of insulin receptor binding" (*id.* at 15651). The reference further goes on to describe that the loss of interaction between Tyr^{60} and Ile^{43} of insulin, as well as moderate conformational changes in the receptor binding region, will affect IGF receptor binding (*id.*).

Thus, claims directed to the use of Y60L or another null IGF having a non-aromatic amino acid at position 60 for the treatment of prostate cancer are enabled.

Lastly, the examiner stated that "rodents are better predictors of human reaction to cardiovascular or anti-inflammatory agents than cancer..." (office action at 4) and that "cancer animal models and cell models, although provide valuable information for delivery of therapeutics, *do not correlate to human in-vivo efficacy*" (office action at 5). While no animal model is 100% predictive of the human condition, one can not correctly conclude that efficacy of a therapeutic agent in an animal model bears zero correlation with therapeutic efficacy in a person. Certainly, none of the references indicate that there is no association between the pathogenesis of cancer in an animal model and a human. Nevertheless, applicant

submits herewith references that describe the use of xenograft models and the use of a PC-3 xenograft animal model as a model for prostate cancer. *See*, Exhibit B.

CONCLUSION

Applicant submits that this application is in condition for allowance and solicits an early indication to that effect. Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, a telephone call to the undersigned is courteously invited.

Respectfully submitted,

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